

PUB. COUNTRY: Jul 16) 224 (2) 438-43.
Journal code: 9Y8; 0372516. ISSN: 0006-291X.
United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199608
ENTRY DATE: Entered STN: 19960912
Last Updated on STN: 19960912
Entered Medline: 19960830

AB We have developed synthetic peptide analogs to analyze novel surface structures of the human **CD4** protein potentially involved in T cell activation. Linear and cyclic peptides derived from the FG and CC' loops of the membrane proximal fourth domain of **CD4** displayed inhibitory activities in a **CD4**-dependent immunological assay. These results suggest that the fourth domain of **CD4** plays an important role in T cell activation. In addition, we report the synthesis of a highly stable **CD4** peptide analog cyclized by the formation of an amide bond between amino and carboxyl termini. Serum stability studies showed that this main-chain cyclic **CD4** peptide was highly resistant to proteolytic degradation while the linear and disulfide cyclic peptides were much less stable. The strategy of main chain cyclization of **CD4** peptides may represent a promising approach to generate proteolytically stable, orally active immunoregulatory agents.

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:n

=> dis his
(FILE 'HOME' ENTERED AT 19:14:08 ON 05 APR 2002)
FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 19:14:24 ON 05 APR 2002
L1 0 S NSNQIC
L2 3 S CNSNQIC
L3 0 S NSNQI
L4 8775 S KORNGOLD R?/AU OR HUANG Z?/AU
L5 195 S L4 AND CD4?
L6 16 S L5 AND LOOP
L7 7 DUP REM L6 (9 DUPLICATES REMOVED)

=>

=> s NSNQI

L3 0 NSNQI

=> dis 12 1-3 ibib abs

L2 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2002 ACS

Full	Citing
Text	References

ACCESSION NUMBER: 1999:578908 CAPLUS
 DOCUMENT NUMBER: 132:152124
 TITLE: Design of peptidic and non-peptidic CD4 inhibitors as novel immunotherapeutic agents
 AUTHOR(S): Li, S.; Satoh, T.; Friedman, T. M.; Gao, J.; Edling, A. E.; Townsend, R.; Koch, U.; Choksi, S.; Han, X.; Shan, S.; Aramini, J. M.; German, M. W.; Korngold, R.; Huang, Z.
 CORPORATE SOURCE: Kimmel Cancer Institute, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA, 19107, USA
 SOURCE: Pept. Sci.: Present Future, Proc. Int. Pept. Symp., 1st (1999), Meeting Date 1997, 797-800. Editor(s): Shimonishi, Yasutsugu. Kluwer: Dordrecht, Neth.
 CODEN: 68BYA5
 DOCUMENT TYPE: Conference
 LANGUAGE: English
 AB A symposium on the authors' work on cyclic peptide c(CNSNQIC) and Tju103 as title inhibitors.
 REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS

Full	Citing
Text	References

ACCESSION NUMBER: 1999:396674 CAPLUS
 DOCUMENT NUMBER: 131:227629
 TITLE: A cyclic heptapeptide mimics CD4 domain 1 CC' loop and inhibits CD4 biological function
 AUTHOR(S): Satoh, Takashi; Aramini, James M.; Li, Song; Friedman, Thea M.; Gao, Jimin; Edling, Andrea E.; Townsend, Robert; Koch, Ute; Choksi, Swati; Germann, Markus W.; Korngold, Robert; Huang, Ziwei
 CORPORATE SOURCE: Kimmel Cancer Institute, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA, 19107, USA
 SOURCE: Pept. Proc. Am. Pept. Symp., 15th (1999), Meeting Date 1997, 609-610. Editor(s): Tam, James P.; Kaumaya, Pravin T. P. Kluwer: Dordrecht, Neth.
 CODEN: 67UCAR
 DOCUMENT TYPE: Conference
 LANGUAGE: English
 AB To search for potential CD4 functional epitopes that could be targeted for the design of new inhibitors, a computer anal. was done conducted for the CD4 D1 domain in conjunction with synthetic peptide mapping. This led to the identification of a surface pocket potentially involved in the CD3-MHC class II interaction. A cyclic peptide, cyclo(CNSNQIC), was designed as a CD4 D1 domain CC' loop mimic. The cyclic peptide blocked CD4-class II-dependent cell rosetting, had immunosuppressive activity, and resisted proteolytic degrdn.
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

Full Text	Citing References
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ACCESSION NUMBER: 2001:320063 BIOSIS
 DOCUMENT NUMBER: PREV200100320063
 TITLE: A CD4 peptide analog enhances engraftment in a murine model of bone marrow transplantation with sublethal conditioning.
 AUTHOR(S): Varadi, Gabor (1); Friedman, Thea M. (1); Korngold, Robert (1)
 CORPORATE SOURCE: (1) Kimmel Cancer Institute, Jefferson Medical College, Philadelphia, PA USA
 SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 375a. print.
 Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
 ISSN: 0006-4971.

DOCUMENT TYPE: Conference

LANGUAGE: English

SUMMARY LANGUAGE: English

AB CD4+ T cells can participate in the process of hematopoietic stem cell graft rejection, particularly when the transplants are performed across a MHC class II barrier. In order to enhance donor marrow engraftment, we tested the efficacy of a small synthetic cyclic heptapeptide - 802.2 (CNSNQIC), which was designed to closely mimic the CD4 domain 1 CC' surface loop, theoretically involved in CD4/MHC class II complex oligomerization and subsequent CD4+ T cell activation. Previously, this peptide was found to have inhibitory activity in murine models for CD4+ T cell-dependent graft-vs-host disease and skin allograft rejection. For a marrow rejection model, we utilized the bm12 -> B6.Ly-5.2 strain combination with sublethal irradiation conditioning and a T cell-depleted bone marrow transplant. Recipients were administered either PBS or a single dose of 802.2 peptide (0.5 mg i.v.) or anti-CD4 mAb (25 mcL i.p.) in a volume of 0.2 mL. Donor-host chimerism was assessed 1-2 months post-transplant by flow cytometric analysis of spleen and/or lymph node cells. Both 802.2 peptide- and anti-CD4 mAb-treated recipients exhibited enhanced donor lymphoid engraftment, with 70-80% and 80-90% donor chimerism, respectively, as compared to 20-30% for the PBS-treated control mice. Furthermore, engraftment of donor hematopoietic progenitor cells in the spleens of recipients was assessed by a 6-day GM-CFU-assay. 802.2 peptide-treated animals yielded enhanced numbers of donor colonies as compared to PBS-treated control recipients. Thus, mice treated with sublethal irradiation in combination with the 802.2 peptide demonstrated increased donor marrow cell engraftment and suggests that this agent may be useful in immunomodulating regimens to overcome MHC class II mismatch barriers in hematopoietic stem cell transplantation.

=> s korngold R?/au or Huang Z?/au
 L4 8775 KORNGOLD R?/AU OR HUANG Z?/AU

=> s 14 and CD4?
 L5 195 L4 AND CD4?

=> s 15 and loop
 L6 16 L5 AND LOOP

=> dup rem 16
 PROCESSING COMPLETED FOR L6
 L7 7 DUP REM L6 (9 DUPLICATES REMOVED)

=> dis 17 1-7 ibib abs
 L7 ANSWER 1 OF 7 MEDLINE

DUPPLICATE 1

Full Text	Citing References
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ACCESSION NUMBER: 2001088949 MEDLINE
 DOCUMENT NUMBER: 20562818 PubMed ID: 11108940
 TITLE: Effect of a cyclic heptapeptide based on the human CD4 domain 1 CC' loop region on murine experimental allergic encephalomyelitis: inhibition of both primary and secondary responses.
 AUTHOR: Edling A E; Choksi S; Huang Z; Korngold R
 CORPORATE SOURCE: Department of Microbiology and Immunology, Jefferson Medical College, 233 S. 10th Street, Philadelphia, PA 19107, USA.
 CONTRACT NUMBER: AI40081 (NIAID)
 NS34928 (NINDS)
 T32CA72318 (NCI)
 SOURCE: JOURNAL OF NEUROIMMUNOLOGY, (2001 Jan 1) 112 (1-2) 115-28.
 Journal code: HSO. ISSN: 0165-5728.
 PUB. COUNTRY: Netherlands
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200101
 ENTRY DATE: Entered STN: 20010322
 Last Updated on STN: 20010322
 Entered Medline: 20010118

AB The 802-2 peptide, designed from the conserved D1-CC' loop region of human CD4, can disrupt CD4(+) T cell activation in both human and murine systems. Here, 802-2 was investigated for efficacy in acute murine experimental allergic encephalomyelitis (EAE) models, and was found to significantly reduce the severity of disease when administered either before or after the onset of symptoms. 802-2 treatment during PLP139-151 induction of EAE rendered the mice more resistant to subsequent rechallenge with antigen, and was also efficacious when initially administered during a secondary EAE response. T cells from 802-2-treated mice proliferated poorly to in vitro restimulation with PLP139-151 and exhibited decreased frequencies of IL-2, IL-4, and IFN-gamma producing cells, but were still able to respond to third-party antigens. These combined results suggest the potential therapeutic value of 802-2 for inhibition of CD4(+) T cell neuroimmunological responses.

L7 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

Full Text Citing References

ACCESSION NUMBER: 2001:320063 BIOSIS
 DOCUMENT NUMBER: PREV200100320063
 TITLE: A CD4 peptide analog enhances engraftment in a murine model of bone marrow transplantation with sublethal conditioning.
 AUTHOR(S): Varadi, Gabor (1); Friedman, Thea M. (1); Korngold, Robert (1)
 CORPORATE SOURCE: (1) Kimmel Cancer Institute, Jefferson Medical College, Philadelphia, PA USA
 SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 375a. print.
 Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology . ISSN: 0006-4971.
 DOCUMENT TYPE: Conference
 LANGUAGE: English
 SUMMARY LANGUAGE: English
 AB CD4+ T cells can participate in the process of hematopoietic stem cell graft rejection, particularly when the transplants are performed across a MHC class II barrier. In order to enhance donor marrow engraftment, we tested the efficacy of a small synthetic cyclic heptapeptide - 802.2 (CNSNQIC), which was designed to closely mimic the CD4 domain 1 CC' surface loop, theoretically involved in CD4/MHC class II complex

oligomerization and subsequent CD4+ T cell activation. Previously, this peptide was found to have inhibitory activity in murine models for CD4+ T cell-dependent graft-vs-host disease and skin allograft rejection. For a marrow rejection model, we utilized the bm12 → B6.Ly-5.2 strain combination with sublethal irradiation conditioning and a T cell-depleted bone marrow transplant. Recipients were administered either PBS or a single dose of 802.2 peptide (0.5 mg i.v.) or anti-CD4 mAb (25 μg i.p.) in a volume of 0.2 ml. Donor-host chimerism was assessed 1-2 months post-transplant by flow cytometric analysis of spleen and/or lymph node cells. Both 802.2 peptide- and anti-CD4 mAb-treated recipients exhibited enhanced donor lymphoid engraftment, with 70-80% and 80-90% donor chimerism, respectively, as compared to 20-30% for the PBS-treated control mice. Furthermore, engraftment of donor hematopoietic progenitor cells in the spleens of recipients was assessed by a 6-day GM-CFU-assay. 802.2 peptide-treated animals yielded enhanced numbers of donor colonies as compared to PBS-treated control recipients. Thus, mice treated with sublethal irradiation in combination with the 802.2 peptide demonstrated increased donor marrow cell engraftment and suggests that this agent may be useful in immunomodulating regimens to overcome MHC class II mismatch barriers in hematopoietic stem cell transplantation.

L7 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:396674 CAPLUS
 DOCUMENT NUMBER: 131:227629
 TITLE: A cyclic heptapeptide mimics CD4 domain 1 CC' loop and inhibits CD4 biological function
 AUTHOR(S): Satoh, Takashi; Aramini, James M.; Li, Song; Friedman, Thea M.; Gao, Jimin; Edling, Andrea E.; Townsend, Robert; Koch, Ute; Choksi, Swati; Germann, Markus W.; Korngold, Robert; Huang, Ziwei
 CORPORATE SOURCE: Kimmel Cancer Institute, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA, 19107, USA
 SOURCE: Pept. Proc. Am. Pept. Symp., 15th (1999); Meeting Date 1997, 609-610. Editor(s): Tam, James P.; Kaumaya, Pravin T. P. Kluwer: Dordrecht, Neth.
 DOCUMENT TYPE: Conference
 LANGUAGE: English
 AB To search for potential CD4 functional epitopes that could be targeted for the design of new inhibitors, a computer anal. was done conducted for the CD4 D1 domain in conjunction with synthetic peptide mapping. This led to the identification of a surface pocket potentially involved in the CD3-MHC class II interaction. A cyclic peptide, cyclo(CNSNQIC), was designed as a CD4 D1 domain CC' loop mimic. The cyclic peptide blocked CD4-class II-dependent cell rosetting, had immunosuppressive activity, and resisted proteolytic degrdn.
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1998:788733 CAPLUS
 DOCUMENT NUMBER: 130:33013
 TITLE: CD4-derived peptides that inhibit immune responses
 INVENTOR(S): Korngold, Robert; Huang, Ziwei
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S., 27 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5846933	A	19981208	US 1996-672610	19960628

OTHER SOURCE(S): MARPAT 130:33013

AB The invention concerns a method of identifying compds. that can be used to inhibit undesired human CD4+-T cell immune responses by identifying compds. that block the interaction of CD4 and MHC class II gene products, as well as a method of treatment which comprises administering such an identified compd. The compds. that inhibit undesired human CD4+-T cell immune responses can be used to treat disease such as multiple sclerosis and to prevent graft rejection and graft vs. host disease. More specifically, the application concerns compds. having mol. wts. between about 1400 and 400 that mimic three portions of the human, CD4 lymphocyte cell-surface antigen. The portions are residues 29-35, the C-C' loop of the D1 domain; residues 317-323, the C-C' loop of the D4 domain; and residues 346-353, the CDR3 or FG ridge of the D4 domain of the CD4 mol. Specific examples of such compds. include cyclic peptides and peptidomimetics.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2002 ACS

Full Text	<input checked="" type="checkbox"/> Citing References
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ACCESSION NUMBER: 1997:181140 CAPLUS
 DOCUMENT NUMBER: 126:166484
 TITLE: CD4-derived peptides and peptidomimetics that inhibit CD4 T-cell immune responses
 INVENTOR(S): Korngold, Robert; Huang, Ziwei
 PATENT ASSIGNEE(S): Thomas Jefferson University, USA; Korngold, Robert; Huang, Ziwei
 SOURCE: PCT Int. Appl., 65 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9701350	A1	19970116	WO 1996-US11176	19960628
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IL, IS, JP, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2226017	AA	19970116	CA 1996-2226017	19960628
AU 9664064	A1	19970130	AU 1996-64064	19960628
EP 835125	A1	19980415	EP 1996-923591	19960628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11510792	T2	19990921	JP 1996-504613	19960628
<u>PRIORITY APPLN. INFO.:</u>				
US 1995-710P P 19950629				
US 1995-4034P P 19950920				
WO 1996-US11176 W 19960628				

OTHER SOURCE(S): MARPAT 126:166484

AB A method is disclosed for identifying compds. that can be used to inhibit undesired human CD4+ T-cell immune responses by identifying compds. that block the interaction of CD4 and MHC class II gene products; also provided is a method of treatment which comprises administering such an

identified compd. that inhibit undesired human **CD4+** T-cell immune responses can be used to treat disease such as multiple sclerosis and to prevent graft rejection and graft vs. host disease. More specifically, compds. are disclosed having mol. wts. of approx. 400-1400 that mimic three portions of the human **CD4** lymphocyte cell surface antigen. The portions are residues 29-35, the C-C' **loop** of the D1 domain; residues 317-323, the C-C' **loop** of the D4 domain; and residues 346-353, and CDR3 or FG ridge of the D4 domain of the **CD4** mol. Specific examples of such compds. include cyclic peptides and peptidomimetics.

L7 ANSWER 6 OF 7 MEDLINE DUPLICATE 2

Full Text	Citing References
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ACCESSION NUMBER: 97277368 MEDLINE
 DOCUMENT NUMBER: 97277368 PubMed ID: 9115290
 TITLE: Bioactive peptide design based on protein surface epitopes. A cyclic heptapeptide mimics **CD4** domain 1 CC' **loop** and inhibits **CD4** biological function.
 AUTHOR: Satoh T; Aramini J M; Li S; Friedman T M; Gao J; Edling A E; Townsend R; Koch U; Choksi S; Germann M W; **Korngold R; Huang Z**
 CORPORATE SOURCE: Kimmel Cancer Institute, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania 19107, USA.
 CONTRACT NUMBER: AI40081 (NIAID)
 NS34928 (NINDS)
 SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 May 2) 272 (18) 12175-80.
 Journal code: HIV; 2985121R. ISSN: 0021-9258.
 PUB. COUNTRY: United States
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199706
 ENTRY DATE: Entered STN: 19970612
 Last Updated on STN: 20000303
 Entered Medline: 19970602

AB The interaction between **CD4** and major histocompatibility complex class II proteins provides a critical co-receptor function for the activation of **CD4** (+) T cells implicated in the pathogenesis of a number of autoimmune diseases and transplantation responses. A small synthetic cyclic heptapeptide was designed and shown by high resolution NMR spectroscopy to closely mimic the **CD4** domain 1 CC' surface **loop**. This peptide effectively blocked stable **CD4**-major histocompatibility complex class II interaction, possessed significant immunosuppressive activity in vitro and in vivo, and strongly resisted proteolytic degradation. These results demonstrate the therapeutic potential of this peptide as a novel immunosuppressive agent and suggest a general strategy of drug design by using small conformationally constrained peptide mimics of protein surface epitopes to inhibit protein interactions and biological functions.

L7 ANSWER 7 OF 7 MEDLINE DUPLICATE 3

Full Text	Citing References
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ACCESSION NUMBER: 96295506 MEDLINE
 DOCUMENT NUMBER: 96295506 PubMed ID: 8702407
 TITLE: Synthetic peptides derived from the fourth domain of **CD4** antagonize off function and inhibit T cell activation.
 AUTHOR: Satoh T; Li S; Friedman T M; Wiaderkiewicz R; **Korngold R; Huang Z**
 CORPORATE SOURCE: Department of Pharmacology, Kimmel Cancer Institute, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania 19107, USA.
 SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1996)

WEST Search History

DATE: Friday, April 05, 2002

<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
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side by side

DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR

L11	nsnqi\$100	2	L11
L10	nsnqi\$10	2	L10
L9	cnsnqic	1	L9
L8	nsnqi	2	L8
L7	CD4 same (peptide adj mimetic\$4)	5	L7
L6	CD4 near (peptide adj mimetic\$4)	0	L6
L5	L4 and (peptide adj mimetic\$4)	45	L5
L4	CD4 and loop	1265	L4
L3	L2 and loop	9	L3
L2	L1 and cd4	40	L2
L1	(Korngold)[IN] OR (Huang)[IN]	19957	L1

END OF SEARCH HISTORY